

69. (Amended) A synthetic nucleic acid sequence which encodes a human protein wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, and the synthetic nucleic acid sequence comprises a continuous stretch of common codons, which continuous stretch includes at least 60% or more of the codons in the synthetic nucleic acid sequence, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

73. (Amended) A synthetic nucleic acid sequence which encodes a human protein wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, and wherein at least 98% or more of the codons in the sequence encoding the protein are common codons and wherein the protein is at least 90 amino acid residues in length, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

81. (Amended) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

85. (Amended) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or

wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

89. (Amended) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein at least 98% or more of the codons in the sequence encoding the Factor VIII are common codons and the Factor VIII is at least 90 amino acid residues in length, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

97. (Amended) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

100. (Amended) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

103. (Amended) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

wherein at least 98% or more of the codons in the sequence encoding the Factor IX are common

6.10
excluded

codons and the Factor IX is at least 90 amino acid residues in length, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

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11

113. (Amended) A synthetic nucleic acid sequence which encodes a human protein wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B and having the following properties:

(i) the synthetic nucleic acid sequence comprises a continuous stretch of at least 150 codons all of which are common codons;

(ii) the synthetic nucleic acid sequence comprises a continuous stretch of common codons, which continuous stretch includes at least 60% or more of the codons in the synthetic nucleic acid sequence; and

(iii) wherein at least 98% or more of the codons in the sequence encoding the protein are common codons and wherein the protein is at least 90 amino acid residues in length.

114. (Amended) A method for preparing a synthetic nucleic acid sequence which is at least 90 codons in length, comprising:

identifying a non-common codon and a less-common codon in a non-optimized gene sequence which encodes a human protein and is at least 90 codons in length; and

replacing at least 98% of the non-common and less-common codons with a common codon encoding the same amino acid residue as the replaced codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

synthesizing at least two fragments of a nucleic acid sequence, wherein the two fragments encode contiguous portions of a human protein of at least 90 amino acids and wherein both fragments are mRNA optimized; and

joining the two fragments to create a nucleic acid encoding the human protein, such that a non-common codon is not created at a junction point, thereby making the mRNA optimized nucleic acid sequence.

119. (Amended) A method for preparing a synthetic nucleic acid sequence encoding a human protein which is at least 90 amino acid residues in length, comprising identifying non-common codon and less-common codons in the non-optimized nucleic acid sequence encoding a protein of at least 90 amino acid residues in length and replacing at least 98% or more of the non-common and less-common codons of the nucleic acid sequence encoding the protein with a common codon encoding the same amino acid residue as the replaced codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, thereby preparing a synthetic nucleic acid sequence encoding a human protein which is at least 90 amino acid residues in length.

120. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons; is at least 80 base pairs in length; and is free of unique restriction endonuclease sites in the message optimized sequence; and has

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell

polypeptide product

125. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, is at least 80 base pairs in length and is free of unique restriction endonuclease sites in the message optimized sequence; and has

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell;

the primary or secondary cell capable of expressing the human protein or polypeptide product.

130. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein at least 98% or more of the codons in the sequence encoding the protein are common codons and the protein is at least 90 amino acids in length; the nucleic acid sequence is at least 80 base pairs in length and is free of unique restriction endonuclease sites in the message optimized sequence; and has

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell;

the primary or secondary cell capable of expressing the human protein or polypeptide product

135. (Amended) A primary or secondary mammalian cell having an exogenous synthetic nucleic acid sequence which encodes a human protein or a polypeptide wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B, and wherein the synthetic nucleic acid has the following properties: it has a continuous stretch of at least 150 codons all of which are common codons; it has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence; at least 98% or more of the codons in the sequence encoding the protein are common codons and the protein is at least 90 amino acids in length; it is at least 80 base pairs in length and which is free of unique restriction endonuclease sites in the message optimized sequence; and

DNA sequences, sufficient for expression of the exogenous synthetic DNA in the transfected primary or secondary cell;

the primary or secondary cell capable of expressing the human protein or polypeptide product.

In the drawings:

Please add the 2 enclosed drawing sheets (Fig. 14A-B) to the application.